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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,145	12/05/2001	Liora Cahalon	B12/31	4185
7590 02/02/2005				
D'vorah Graeser c/o Anthony Castorina 2001 Jefferson Davis Highway Suite 207 Arlington, VA 22202		EXAMINER HUI, SAN MING R		
		ART UNIT 1617		PAPER NUMBER
DATE MAILED: 02/02/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)		
	10/002,145		CAHALON ET AL.		
	Examiner		Art Unit		
		San-ming Hui	1617		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 04 October 2004.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1,5-13 and 16-35 is/are pending in the application.

4a) Of the above claim(s) 5,6,9,13,22,23,26 and 29 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1,7,8,10-12,16-21,24,25,27,28 and 30-35 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed October 4, 2004 have been entered. The cancellation of claims 2-4, 14-15, and 20 is acknowledged. The addition of claims 33-35 is also acknowledged.

Claims 5, 6, 9, 13, 22, 23, 26, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed February 13, 2004.

Claims 1, 7-8, 10-12, 16-21, 24-25, 27-28, 30-35 are examined to the extent they read on the elected species.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the amendments filed October 4, 2004. The claims are no longer directed to the treatment of all malignancy.

The outstanding rejection under 35 USC 112, second paragraph with regard to the lack of antecedent basis in claims 7 and 24 is withdrawn in view of the amendments filed October 4, 2004.

Priority

Applicant's remarks with regard to the priority have been considered, but are not found persuasive. Examiner notes that the mechanism of action of the recited heparin or heparin sulfate derivatives (i.e., interfering CXCR4 7TM-GPCR signaling pathway) is not supported in the applications in which the instant application claims priority from.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8, 10, 16-19, 21, 25, and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "sulfated glucosamine derivative of heparin or heparin-sulfate" recited in claim 1 renders the claims indefinite because it is not clear what compounds would be considered as sulfated glucosamine derivatives of heparin or heparin-sulfate. Derivatives is usually referred to a compounds that is derived or, in other words, chemically modified from the parent compounds. In the instant case, the term "sulfated glucosamine derivatives of heparin or heparin sulfate" would encompass compounds having sulfated glucosamine moieties and are somehow related to heparin structurally. Therefore, the structure of these compounds, which are encompassed by the term "sulfated glucosamine derivatives of heparin or heparin sulfate", would not be known and therefore, the metes and bounds of the claims would not be ascertained by the skilled artisan.

For essentially the same reason, the expression "an oligosaccharide ... is carboxylated and sulfated" recited in claim 18 renders the claims indefinite because it is not clear what oligosaccharide compounds are encompassed by the claims.

Claim Rejections - 35 USC § 103

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7-8, 10-12, 16-21, 24-25, 27-28, and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over '318 (US patent 4,882,318) in view of Vlodavsky et al. (Adv. Exp. Med. Biol., 992;13:317-327).

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'318 teaches heparin and its related molecules for the treatment of tumor by inhibit heparanase activity and thereby decrease the metastasis of the tumor, especially lung cancer (See the abstract, col. 1 – 2). '318 teaches the dose of heparin and its related molecules useful for treating tumor metastasis as 50-500 μ g/kg/day (See claim 1).

'318 does not expressly teach the herein oligosaccharide compounds, with the herein claimed molecular weight, for treating lung tumor metastasis.

Vlodavsky et al. teaches to optimize cancer therapy, one would want to chose a heparin compounds that has low potential for bFGF release but a high inhibition of heparanase activity (See page 317-320). Vlodavsky et al. teaches various factors would affect the heparanase inhibition activity and the bFGF release activity. Those factors are the size, sulfation, acetylation, the position where sulfation or desulfation of the heparin molecules (usually at the N- position) (See page 321-324, particularly, Fig. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the herein claimed heparin molecules, with the herein claimed molecular weight, for the treatment of lung cancer.

One of ordinary skill in the art would have been motivated to employ the herein claimed heparin molecules, with the herein claimed molecular weight, for the treatment of lung cancer. From the teachings of the cited prior art, modifying heparin oligosaccharide compounds with different sulfation at the N- position to the herein claimed heparin oligosaccharide compounds in order to maximized the heparanase

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inhibition, which is the mechanism to reduce tumor metastasis, would be reasonably expected to be useful in reducing tumor metastasis and thereby treating cancer.

Furthermore, optimizing the number of saccharide units in the herein claimed heparin molecules would have been reasonably expected to be effective in minimize the undesirable effects and at the same time to maximize the therapeutic effect.

Response to arguments

Applicant's arguments filed October 4, 2004 averring Vlodavsky et al.'s failure to teach the oligosaccharides with more than 10 units as effectively in treating tumor metastasis have been considered, but are not found persuasive. Firstly, although Vlodavsky teaches the inhibition of tumor metastasis would be best achieved by oligosaccharides with 16 or more sugar units, Vlodavsky does not exclude oligosaccharides with less than 10 units would be ineffective in treating tumor metastasis. Furthermore, it is known that the release of bFGF would result in angiogenesis. From the result of Fig. 1, oligosaccharides with higher number of sugar units would tend to induce more release of bFGF. Therefore, it would be reasonably expected to maximize the tumor metastasis inhibition effect (therapeutic effect) while minimize the release of bFGF (undesirable effect) by adjusting the length of sugar unit and the sulfation of the heparin compound. Therefore, absent evidence to the contrary, possessing the teachings of the cited prior arts, one of ordinary skill in the art would be reasonably expected to optimize the length of the sugar unit in the oligosaccharide compound.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



San-ming Hui
Primary Examiner
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